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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/230,929	04/02/1999	JURGEN KLEINSCHMIDT	4121-107	3634

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INTELLECTUAL PROPERTY / TECHNOLOGY LAW
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EXAMINER
WOITACH, JOSEPH T

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 01/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/230,929	Kleinschmidt et al.
Examiner	**Art Unit**
Joseph Woitach	1632

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) [X] Responsive to communication(s) filed on *Oct 10, 2002* .

2a) [ ] This action is **FINAL**. 2b) [X] This action is non-final.

3) [ ] Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) [X] Claim(s) *14-25, 27, 29, 38-61, 65, and 66* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) [ ] Claim(s) _____ is/are allowed.

6) [X] Claim(s) *14-25, 27, 29, 38-61, 65, and 66* is/are rejected.

7) [ ] Claim(s) _____ is/are objected to.

8) [ ] Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) [ ] The specification is objected to by the Examiner.

10) [ ] The drawing(s) filed on _____ is/are a) [ ] accepted or b) [ ] objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) [ ] The proposed drawing correction filed on _____ is: a) [ ] approved b) [ ] disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) [ ] The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) [X] Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) [ ] All b) [ ] Some* c) [X] None of:

1. [ ] Certified copies of the priority documents have been received.
2. [ ] Certified copies of the priority documents have been received in Application No. _____ .
3. [X] Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) [ ] Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) [ ] The translation of the foreign language provisional application has been received.

15) [ ] Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) [X] Notice of References Cited (PTO-892)
2) [ ] Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) [ ] Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) [ ] Interview Summary (PTO-413) Paper No(s). _____
5) [ ] Notice of Informal Patent Application (PTO-152)
6) [ ] Other:

DETAILED ACTION

This application is a 371 national stage filing of PCT/DE97/01629, filed July 30, 1997, which claims benefit to foreign application 196 31 357.0, filed August 2, 1996 in Germany.

Applicants' amendment filed October 15, 2002, paper number 26 has been received and entered. Claims 14, 38-50 and 65 have been amended. Claims 26, 28 and 30-37 have been canceled. Claims 14-25, 27, 29, 38-61, 65 and 66 are pending and currently under examination.

Priority

Acknowledgment is made of Applicant's claim for foreign priority based on an application filed in Germany on August 2, 1996. It is noted, however, that applicant has not filed a certified copy of the German application as required by 35 U.S.C. 119(b).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 14-25, 27, 29, 38-61, 65 and 66 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically:

Claims 14, 49, 50- 53 and 65 recite the limitation "the structural ORF" however there is no prior recitation in the claim for this embodiment. It is noted that the first component described is directed to a structural papillomavirus polypeptide, not an ORF. There is insufficient antecedent basis for this limitation in the claim. Additionally, the claims are unclear in the recitation of "a non-transforming ORF" because an ORF is not transforming, rather it is the polypeptide encoded by the ORF which could be non-transforming.

Claims 43-48 are unclear in the recitation of "and structural papillomavirus polypeptide" because it is not clear if the claim refers to the papillomavirus polypeptide recited in the claim on which they depend or if it is directed to additional polypeptides. Amending the claims to recited "the structural..." would obviate the basis of the rejection.

Claims 50 and 54-59 recite the limitation "the human papillomavirus of (a) and (b) is selected" however there is no prior recitation for (a) nor (b). It is noted that the two components are described however neither are identified by a letter indication. There is insufficient antecedent basis for this limitation in the claim.

Claims 38-48 have been newly amended to recite "non-transforming E6-ORF" and "non-transforming E7-ORF", respectively. The claims are unclear in the recitation of "non-transforming" because neither E6 nor E7 are recognized to be transforming proteins. The present specification teaches as a preferred polypeptide that is "non-transforming" the proteins encoded by the E6 and E7-ORFs (page 3, second full paragraph). As further more specific evidence for what was known in the art, in reviewing HPV Swan *et al.* (Arch Virol, 1994) teach that

transfection "of E6 and E7 genes from the oncogenic HPV types into primary rodent cells causes immortalization, but not transformation" (page 110, second full paragraph). The claims are unclear and confusing because it is not clear how "non-transforming" further limits the claims or the inherent properties of E6 and E7.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 14-25, 27, 29, 38-61, 65 and 66 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Whittle *et al.* ('087), Donelly *et al.* ('785) and Johnson (96/00583) for reasons of record set forth in the previous office actions of June 13, 2002, paper number 24.

Applicants summarize the invention and note the withdrawal the 35 USC 103 rejection over Donelly *et al.* ('785) and Johnson (96/00583). Noting the reasons for withdrawing the previous rejection as it applies to the instant rejection, Applicants argue that Donelly *et al.* teaches away from using the AAV vectors disclosed in Johnson. Specifically, Applicants point to teachings in Donelly *et al.* that retroviral vectors have certain limitations which make them less suitable as a delivery vehicle for DNA vaccines and for the teaching of the preferred use of artificially engineered plasmids (pages 7-8). With respect to Whittle *et al.* Applicants argue that no specific motivation for use of an AAV vector system is provided (page 9). Noting the recent court decision of *In re Lee*, Applicants argue that a *prima facie* case has not been established because the rejection fails to provide the motivation to combine the prior art references (pages 10-11). Additionally, Applicants note that neither reference teach using **non-transforming** E6-ORF or E7-ORF (pages 8-9). See Applicants' amendment, pages 6-12. Applicants' arguments have been fully considered but not found persuasive.

Initially, with respect to the lack of teaching of any of the references for using a "non-transforming" E6- or E7-ORFs, Applicants arguments not found persuasive. First, it is noted that neither of these sequences are considered transforming in the art. As evidence to this fact, Swan *et al.* (Arch Virol, 1994) teach that transfection "of E6 and E7 genes from the oncogenic HPV types into primary rodent cells causes immortalization, **but not transformation**" (emphasis added, page 110, second full paragraph). The courts have stated that reliance upon inherency is not improper even though rejection is based on Section 103 instead of Section 102. *In re Skoner*,

et al. 186 USPQ 80 (CCPA). Second, the present specification as a preferred polypeptide that is "non-transforming" specifically teaches the proteins encoded by the E6 and E7-ORFs (page 3, second full paragraph). A review of the entire disclosure does not indicate that these ORF were considered transforming, nor if they were considered such, any teaching on how to modify these sequences to be "non-transforming". Applicants' arguments are not found persuasive because the specification teaches the preferred use of E6 and E7 as non-transforming proteins in the context of the claimed invention, and the art recognizes E6 and E7 as non-transforming.

With respect to Applicants arguments that Donelly *et al.* teaches away from the present invention, Examiner acknowledges the specific portions of Donelly *et al.* cited, however, none of these specifically teach away from the claimed invention. As noted in the previous rejection Donelly *et al.* generally supports the use of any vector (see previous action paper number 24, pages 4-6). Examiner notes that plasmids are preferred embodiment taught by Donelly *et al.* because they do not replicate, however this does not teach away from the use of other vectors which do not replicate. Also, the limitations for the use of retroviruses is noted, however AAV is not a retrovirus (it is a replication deficient ssDNA parvorvirus), nor does it have the limitations set forth by Donelly *et al.* for a retrovirus vector. The teachings pointed to by Applicants provide a general knowledge of the art for various vectors which are known at the time of filing. At the time of filing, Johnson teaches that the AAV vectors were known and used for delivering DNA vaccines. An AAV vector is replication deficient which a solution to the problem acknowledged by Donelly *et al.* for the use of a retrovirus. Further, Johnson teaches the artisan

is capable of removing all but the ITR for the insertion of heterologous sequences into an AAV genome. Finally, Johnson teaches the insertion of multiple and varied viral sequences which could serve in the context of a DNA vaccine. Applicants' arguments that Donelly *et al.* teaches away from the use of the AAV vectors of Johnson is not persuasive, because the use of AAV vectors in the context of DNA vaccines for various viruses was known, and the properties of AAV vectors solve problems recognized by the art as set forth in Donelly *et al.* for the use of retroviral vectors.

With respect to Applicants' arguments regarding that the references combined do not teach a **fused polypeptide** comprising a **non-transforming** E6/E7-ORF (page 11, last paragraph), it is noted that Whittle *et al.* specifically teaches an example of the fusion protein of HPV L2 and E7 (see summary in abstract and column 5, lines 47-51). Further, as discussed above in detail, the E6 and E7 are non-transforming. Applicants arguments are not persuasive because there is the specific teaching of a L2-E7 fusion protein by Whittle *et al.* which anticipates the claims.

Finally, Examiner acknowledges the decision of *In re Lee*, however unlike the 'common knowledge' referred to by the court for combining the television system taught in '892 with a handbook manual, the basis of the present rejection relies on the teaching of Donnelly *et al.* for the overall teaching for DNA vaccines expressing HPV antigens and the teaching of Johnson for advantageous use of AAV vectors for DNA vaccines against viral antigens. Whittle *et al.* provides the specific teaching that at the time of filing HPV fusion proteins were used as

vaccines and could be expressed by a vector. As noted in the previous office action, all of the references are related in the art as they are drawn to providing vaccines. More specifically, the references provide the necessary and specific teachings for the generation of HPV antigens administered as a DNA vaccine. The motivation for the combination of the references is to provide for an effective DNA vaccine, in this case the advantage of a non-replicating AAV vector which is capable of infecting all cell types in a subject for the delivery of known papilloma virus antigens to a subject. In this case there has been no reliance on common knowledge to make the instant rejection or conclusory statements for combining non-analogous art, as was the case in *In re Lee*.

Thus, for the reasons above and of record, the claimed invention as a whole was clearly *prima facie* obvious, and therefore, the rejection is maintained.

Claims 16, 18, 20 and 50 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Whittle *et al.* ('087), Donelly *et al.* ('785) and Johnson (96/00583) in further view of Gissmann *et al.* (96/11272) for reasons of record set forth in the previous office actions of June 13, 2002, paper number 24.

Applicants summarize the teaching of Gissmann *et al.* and argue that the reference must be viewed for the teaching as a whole and that the teachings for the fusion proteins in Gissmann *et al.* is contrast to that taught in Donnelly *et al.* See Applicants' amendment, pages 12-13. Applicants' arguments have been fully considered but not found persuasive.

Gissmann *et al.* was relied upon to provide that at the time of filing that various HPV strains were known as well as the early and late ORFs. It is noted that Whittle *et al.* recognizes the existence of a variety of HPV strains (column 1, lines 40-45), however they do encompass all those recited in the instant claims. The reliance on Gissmann *et al.* was to provide evidence of what was well known in the art, in particular the specific HPV strains to make obvious each of the limitations in the claims. Applicants' arguments that the artisan would not combine Gissmann *et al.* because the fusion proteins generated are not the same as disclosed by Whittle *et al.* is unpersuasive because Gissmann *et al.* is not relied upon for this teaching.

Thus, for the reasons above and of record, the claimed invention as a whole was clearly *prima facie* obvious, and therefore, the rejection is maintained.

Claims 61 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Whittle *et al.* ('087), Donelly *et al.* ('785) and Johnson (96/00583) in further view of Stanley *et al.* ('869)for reasons of record set forth in the previous office actions of June 13, 2002, paper number 24.

Applicants' argue that regardless of the teachings of Stanley *et al.* the deficiencies of Whittle *et al.*, Donelly *et al.* and Johnson are not remedied. See Applicants' amendment, page 13. Applicants' arguments have been fully considered but not found persuasive.

Like Gissmann *et al.*, Stanley *et al.* is relied upon to teach what was known in the art, specifically that one or more immune system activators can be administered to augment the effectiveness of the vaccine. Stanley *et al.* teach that IL-12 can be administered with HPV

antigens or a vector encoding said antigens (summarized in abstract). It is noted that Stanley *et al.* even cites Donnelly *et al.* as a means known in the art as polynucleotide vaccine (column 6, lines 65-67). Applicants arguments are not found persuasive because Stanley *et al.* relied upon only for teaching a more effective vaccine by providing IL-12 to a subject, and not required for the *prima facie* case over Whittle *et al.*, Donelly *et al.* and Johnson.

Thus, for the reasons above and of record, the claimed invention as a whole was clearly *prima facie* obvious, and therefore, the rejection is maintained.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (703)305-3732.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (703)305-4051.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (703) 308-2141.

Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers

must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center numbers are (703)308-4242 and (703)305-3014.

Joseph T. Woitach

RAM R. SHUKLA, PH.D
PATENT EXAMINER